The first vanadium-catalyzed oxidation of aryl allylic selenides with *in situ* [2,3] sigmatropic rearrangement†

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The efficient synthesis of a series of 2° allylic alcohols from a vanadium-catalyzed oxidation of suitably disposed allylic selenides with tandem [2,3] sigmatropic rearrangement is outlined.

The rapid growth of metal-catalyzed transformations in recent decades has contributed to the construction of evermore complex synthetic targets. For example, the catalytic oxidation of sulfides is well documented using several transition metal catalysts.[1] This methodology has proven useful in both racemic and enantioselective pathways. Recently, Bolm and co-workers showcased the use of vanadium for the enantioselective oxidation of prochiral sulfides.[2] In addition, the Ellman laboratory has reported an elegant use of a similar catalytic system for the enantioselective oxidation of alkyl disulfides.[3] Despite these encouraging results, relatively little attention has been paid to the corresponding oxidation of selenium. In particular, the tandem oxidation of suitably disposed allylic selenides with *in situ* [2,3] sigmatropic rearrangement has been limited to stoichiometric oxidants such as oxaziridines, peracids or peroxides.[4] Scattered asymmetric methods have also been developed for these transformations utilizing primarily stoichiometric titanium–tartrate complexes[5] or chiral oxaziridines.[6] In addition, several groups have studied the effect of a chiral auxiliary on selenium.[7] None of these systems, however, have been exploited in a sub-stoichiometric sense for this transformation.[8] We herein report the first catalytic method for oxidation of allylic selenides with tandem *in situ* [2,3] sigmatropic rearrangement.

Our initial exploits in this area were directed toward the use of titanium-mediated oxidation based on previously described conditions;[9] however, this proved to be ineffective in our hands due to lack of generality, slow reaction times, and the need for stoichiometric amounts of the metal catalyst. Our interest then turned to the use of vanadyl(iv) acetylacetonate as a potential candidate for the desired transformation. Synthesis of the selenide precursors was readily accomplished from the corresponding alcohol using tributylphosphine and *o*-nitrophenyl selenocyanate in high yield.[10]

The standard reaction conditions involved a 0.3 M solution of the selenide **1** in methylene chloride with vanadyl(iv) acetylacetonate (10 mol%) in the presence of powdered 4 Å molecular sieves (Scheme 1). This green solution was then cooled to −10 °C in an ice–acetone bath and cumene hydroperoxide (1.8 equiv.) was added to the stirred solution. After the reaction was judged to be complete, tributylphosphine (1.2 equiv.) was added to convert the intermediate selenenate **3** to the desired allylic alcohol **4**. This efficient and rapid method for cleavage of the selenenate species **3** is noteworthy because of its tolerance for sterically demanding systems such as the adamantyl selenide **1c**. Previous described methods for selenenate cleavage (such as pyridine and water) proved to be slow and capricious in our hands. The vanadium metal catalyst is
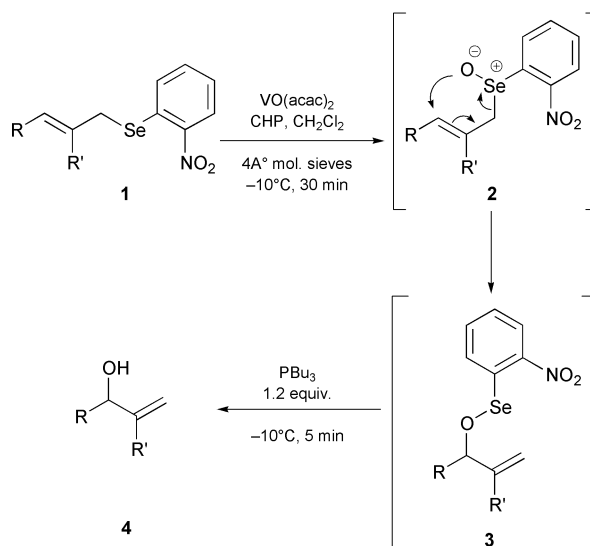
Scheme 1 Selenide oxidation, sigmatropic rearrangement and selenenate cleavage sequence.

critical for the dual reaction sequence to proceed; the blank experiment without VO(acac)$_2$ resulted in no conversion of the selenide under the prescribed reaction conditions.[11] It has been previously reported that phenyl selenides can be oxidized using *tert*-butyl hydroperoxide in the absence of a metal catalyst;[12] however, the decreased reactivity of the selenium to oxidation that is observed may be due to the electron withdrawing nature of the *o*-nitro substituent.

A variety of substituents on the alkene were studied in order to investigate the utility of this methodology as shown in Table 1. These results suggest that the oxidation and rearrangement occur rapidly, regardless of the steric environment located at the allylic position. In addition, the vanadium-mediated conditions occur equally effectively with conjugated and non-conjugated olefins. These results are in contrast to preliminary studies in our laboratory with titanium-mediated reactions in which substitution on the alkene function had a dramatic impact on the efficiency of the reaction. Furthermore, the rearrangement does not seem to be influenced by a stereogenic center located in the allylic position. For example, treatment of selenides **1f** and **5c** yielded the resultant allylic alcohol in nearly 1:1 selectivity. This result is in good agreement with Davis and co-workers who have shown that the stereochemical outcome of the resultant alcohol in acyclic substrates appears to be determined by the oxidation of the selenide.[6] Finally, the results in Table 2 demonstrate that this methodology is equally effective for the *cis* olefin geometry.

In conclusion, the first vanadium-catalyzed method for oxidation of selenides is reported with tandem [2,3] sigmatropic rearrangement. This methodology is effective on a broad range of substrates, regardless of steric environment, thereby expanding the scope and utility of selenoxide rearrangements. Furthermore, tributylphosphine is shown to be a rapid and

Table 1 Selected data for *trans* disposed allylic selenides[a]

Entry	R	R′	Yield[b] (d.s.)
a[c]	CH₃(CH₂)₄–	H	70%
b	cyclohexyl	H	75%
c	adamantyl	H	84%
d	4-MeO-C₆H₄–	H	66%[d]
e	phenyl	CH₃	70%
f	Bn–	H	60% (1.1:1)

[a] All reactions unless otherwise noted were performed at 0.3 M substrate concentration using 1.2 equiv. tributylphosphine to quench the selenenate intermediate. [b] All yields are isolated yields after chromatography over silica gel. [c] This reaction was quenched with triphenylphosphine. [d] *tert*-Butyl hydroperoxide was substituted for cumene hydroperoxide to simplify purification.

Table 2 Selected data for *cis* disposed allyl selenides[a]

Entry	R′	Yield[b] (d.s.)
a[c]	CH₃(CH₂)₄–	89%
b	phenyl	71%[d]
c	Bn–	71% (1.2:1)

[a] All reactions unless otherwise noted were performed at 0.3 M substrate concentration using 1.2 equiv. tributylphosphine to quench the selenenate intermediate. [b] All yields are isolated yields after chromatography over silica gel. [c] This reaction was quenched with triphenylphosphine. [d] *tert*-Butyl hydroperoxide was substituted for cumene hydroperoxide to simplify purification.

general method for selenenate cleavage and a viable alternative to traditional methods. In addition, it should be possible to effect catalytic asymmetric oxidation of selenium with tandem sigmatropic rearrangement using the appropriate multidentate ligand–vanadium system. We are actively pursuing this area and will report our results in due course.

The authors wish to thank the University of Mississippi for their generous support of this work.

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